UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/570,122	02/28/2006	Christine Power	ARS.122	7430

23557 7590 01/14/2011

SALIWANCHIK, LLOYD & EISENSCHENK
A PROFESSIONAL ASSOCIATION
PO Box 142950
GAINESVILLE, FL 32614

EXAMINER	
DEBERRY, REGINA M	

ART UNIT	PAPER NUMBER
1647	

NOTIFICATION DATE	DELIVERY MODE
01/14/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

euspto@slspatents.com

Office Action Summary	Application No.	Applicant(s)	
	10/570,122	POWER ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 November 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *46-50,55 and 57-86* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46-50,55 and 57-86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/8/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Status of Application, Amendments and/or Claims

The amendment and Applicant's arguments, filed 08 November 2010, have been entered in full. Claims 1-45, 51-54, 56 are canceled. Claims 46-50, 55, 57-86 are under examination.

Information Disclosure Statement

The information disclosure statement(s) (IDS) (filed 08 November 2010) was received and complies with the provisions of 37 CFR §§1.97, 1.98 and MPEP § 609. It has been placed in the application file and the information referred to therein has been considered as to the merits.

Withdrawn Objections And/Or Rejections

The rejection to claim 71 under 35 U.S.C. 112, second paragraph, as set forth at page 2 of the previous Office Action (06 August 2010), is *withdrawn* in view of the amendment (08 November 2010).

Claim Rejections-35 USC § 112, First Paragraph, Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 46-50, 55, 57-86 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a method for treating a fibrotic disease comprising administering to a patient having a fibrotic disease a therapeutically effective amount of a composition comprising

a pharmaceutically acceptable carrier and a polypeptide comprising **SEQ ID NO:2**, wherein said fibrotic disease is lung fibrosis or liver fibrosis

does not reasonably provide enablement for:

a method for treating a fibrotic disease comprising administering to a patient having a fibrotic disease a therapeutically effective amount of a composition comprising a pharmaceutically acceptable carrier and a polypeptide comprising **SEQ ID NO:5 or SEQ ID NO:7**, wherein said fibrotic disease is lung fibrosis or liver fibrosis.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The basis for this rejection is set forth at pages 3-7 of the previous Office Action (06 August 2010).

Applicant argues that the pending claims do not recite fragments and/or mutants of INSP035 full length (corresponding to SEQ ID NO:2) nor polypeptides having random mutations or deletions. Applicant maintains that the claims recite polypeptides comprising or consisting of SEQ ID NOs:5 or 7, i.e. polypeptides comprising or consisting of definite sequences, shown to display activity as SEQ ID NO:2 on TRAIL inhibition *in vitro*. Applicant cites page 7, lines 18-22 and page 27, line 7. Applicant states that it is further noted that Example 5 of the present invention describes an assay for testing the activity of INSPO35 in bleomycin treated mice.

Applicant's arguments have been fully considered but are not found persuasive. The specification teaches the full length cDNA of human INSP035 as SEQ ID NO:1 and

the corresponding amino acid sequence as SEQ ID NO:2 (page 9, lines 23-26). The sequence listing teaches SEQ ID NO:2 as having 163 amino acids. *The specification states that the cDNA of human INSP035 starting at the 2nd methionine from INSP035 has been cloned.* ***This protein is called INSP035 medium form****. The cDNA is SEQ ID NO:4 and* ***the corresponding amino acid sequence is SEQ ID NO:5*** *(page 9, lines 26-29). The sequence listing teaches* ***SEQ ID NO:5 as having 88 amino acid residues.*** The specification teaches that ***a modified INSP035 medium form with an isoleucine substitution at position 1 has been generated as SEQ ID NO:7*** (page 9, lines 29-31). The sequence listing teaches ***SEQ ID NO:7 as having 88 amino acid residues.*** Contrary to Applicant's assertion, the instant claims are drawn to fragments and mutants of INSP035 full length (corresponding to SEQ ID NO:2). Furthermore, the *in vivo* assay (mice model of lung fibrosis) was employed to test the activity of SEQ ID NO:2 ***NOT*** SEQ ID NO:5 or SEQ ID NO:7.

Applicant argues that the as-filed specification fully enables the claimed invention. Applicant argues that the polyhistidine labeled forms of SEQ ID NOs:2, 5 and 7 have been demonstrated to inhibit TRAIL activity. Applicant cites Figure 1 and page 7, lines 18-22). Applicant argues that the specification teaches that the claimed polypeptides are capable of inhibiting TRAIL assay. Applicant notes that the art recognizes that shorter peptides (variants/mutants) retain both *in vivo* and *in vitro* activity. Applicant submits references. Applicant argues that parathyroid hormone (PTH) is a polypeptide comprising 84 residues, known to induce anabolic effects one bone. An N-terminal fragment of PTH, the peptide PTH(1-34), although containing fewer than

one-half the number of amino acids residues as PTH, displays similar *in vivo* effects as compared to PTH. Applicant argues that the second example, leptin, is a polypeptide consisting of 167 residues (the mature form consists of 147 residues), that is well-known for reducing body weight and food intake *in vivo* (see Table 1, page 16 of WO 97/46585). Applicant states that similar *in vivo* effects were shown for a leptin fragment comprising 15 residues (residues 116-130 of leptin). Applicant maintains that this fragment contained fewer than 10% of the amino acid residues found in full length leptin yet exerted similar biologic effects (see Table 7, page 72 and Figure 4J of WO 00/11173).

Applicant's arguments have been fully considered but are not found persuasive. The Examiner did not state that SEQ ID NOs:5 and 7 failed to inhibit TRAIL activity *in vitro*. The Examiner stated that the specification fails to teach that *administered* fragments and/or mutants of full length INSP035 SEQ ID NO:2 (i.e. SEQ ID NOs:5 and 7) treat lung fibrosis or liver fibrosis *in vivo*. Applicant's arguments regarding parathyroid hormone (PTH) and leptin are not found persuasive. The Examiner understands that that the art recognizes that shorter peptides (variants/mutants) can retain both *in vivo* and *in vitro* activity. However, the instant specification fails to teach such for the claimed variant/fragments. Grasso et al. (Endocrinology, Vol. 138/No.4; 1997) teach that the mouse ob gene and its human homologue were cloned in 1994 (page 1413, 1st paragraph). Leptin is the product of this gene. Grasso et al. teach that in genetically obese mice, a nonsense mutation in the ob gene changes the coding sequence for arginine (Arg-105) in normal leptin to a stop codon. The resulting mRNA is

translated into a truncated, inactive leptin. Grasso et al. teach that these observations suggest that leptin activity may be localized in part, toward the C-terminus of the protein (page 1414, 1st column, last paragraph-2nd column, 1st paragraph). Grasso et al. made overlapping **synthetic peptide, which were tested *in vivo*** to map the active domains (Figures 1-4). Grasso et al. teach that peripherally administered synthetic peptides corresponding to restricted domains within the primary structure of leptin are biologically active and have the ability to alter feeding behavior (page 1418, last paragraph). The registered drug of PTH 1-34 (reference submitted by Applicant) was surely tested *in vitro* and *in vivo*.

The PTH and leptin protein have been cloned and fully characterized (i.e. binding domains, catalytic sites). Thus, the more that is known in the prior art about the nature of the invention and the more predictable the art is, the less information needs to be explicitly stated in the specification. If little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and/or use the invention to be enabling. In the instant case, the recited proteins are novel and no catalytic sites/biological domains for inhibiting liver or lung fibrosis have been identified. The specification fails to characterize the active domains in the proteins which are critical to the claimed activity (i.e. anti-fibrotic activity). The specification fails to teach the *in vivo* administration of SEQ ID NOs:5 and 7. The Examiner provided art which demonstrates that just because a variant protein has activity in an *in vitro* assay does not necessarily mean that variant will have the same

activity *in vivo*. The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached on (571) 272-0911. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Marianne P. Allen/
Primary Examiner, Art Unit 1647
/R. M. D./
Examiner, Art Unit 1647
1/10/11